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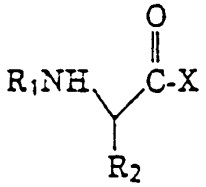
(54) Novel peptidase inhibitors.

(57) This invention relates to analogs of peptidase substrates in which the nitrogen atom of the scissile amide group of the substrate peptide has been replaced by a substituted malonyl moiety.

The contemplated peptidase inhibitors of the foregoing enzymes are selected from the generic formula



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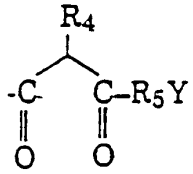
the hydrates, isosteres or the pharmaceutically acceptable salts thereof wherein X is



R_1 is hydrogen, an amino protecting group selected from Group K, an α-amino acid or a peptide comprised of a number of α-amino acid building blocks, said α-amino acid or peptide optionally bearing on its terminal nitrogen atom an amino protecting group selected from Group K,

R_2 is the "R group" residue of the α-amino acid responsible for directing the inhibitor to the active site of the enzyme or is -A-$SiR_7R_8R_9$, C_{1-10} alkyl, aralkyl or aryl with R_7, R_8 and R_9, each being selected from C_{1-10} alkyl, aralkyl or aryl and A is a C_{1-5} alkylene,

R_4 is the specific R-group residue of the α-amino acid for that peptidase substrate analog,

R_5 is an α-amino acid or peptide comprised of α-

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EUROPEAN SEARCH REPORT

Application Number

EP 89 40 2763

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
X	EP-A-0 133 225 (HOFFMANN-LA ROCHE) " Example 5; pages 28-29 "	3	C 07 K 5/02 C 07 K 5/06 C 07 K 5/08 C 07 K 5/10 C 07 C 237/20 A 61 K 37/64
X	CHEMICAL ABSTRACTS, vol. 99, no. 21, 21st November 1983, pages 122-123, 170031x, Columbus, Ohio, US; "Intramolecular cross-linking of insulin. Preparation and properties of oxalyl-and malonyl-bis(methionyl) insulin", & INT. J. PEPT. PROTEIN RES. 1983, 22(2), 214-22 " Abstract "	1,10,14, 24,26,28, 32,34,36, 38	
A	FR-A-2 537 131 (ROQUES et al.) " Whole document "	1-40	

TECHNICAL FIELDS SEARCHED (Int. Cl.5)
C 07 K C 07 C A 61 K

The present search report has been drawn up for all claims

Place of search	Date of completion of search	Examiner
The Hague	19 June 91	MASTURZO P.

CATEGORY OF CITED DOCUMENTS

X: particularly relevant if taken alone
Y: particularly relevant if combined with another document of the same catagory
A: technological background
O: non-written disclosure
P: intermediate document
T: theory or principle underlying the invention

E: earlier patent document, but published on, or after the filing date
D: document cited in the application
L: document cited for other reasons

&: member of the same patent family, corresponding document